

CLAIMS

1. A method for modulating the expression of a genetic sequence wherein said sequence comprises an ORF having an RTG or RUG wherein R is A or G corresponding to an authentic translation site of said ORF and a nucleotide sequence 5' of said authentic translation start site, said method comprising introducing or removing one or more RTG or RUG triplets in said 5' nucleotide sequence upstream of said authentic translation initiation site such that upon expression of said genetic sequence, there is a respective decrease or increase in the level of expression.
2. A method according to Claim 1 wherein the expression is increased by the removal of one or more RTG or RUG triplets, wherein R is A or G in the 5' nucleotide sequence upstream of the authentic translation initiation site.
3. A method according to Claim 1 wherein the expression is decreased by the introduction of one or more RTG or RUG triplets, wherein R is A or G in the 5' nucleotide sequence upstream of the authentic translation initiation site.
4. A method according to Claim 1 or 2 or 3 wherein the RTG or RUG triplets in the 5' nucleotide sequence upstream of the authentic translation initiation site is ATG or AUG.
5. A method according to Claim 4 wherein the triplet is ATG.
6. A method according to Claim 4 wherein the triplet is AUG.
7. A method according to any one of Claims 1 to 6 further comprising introducing or removing one or more termination signals in the 5' nucleotide sequence, the coding sequence or downstream of the authentic translation initiation site and/or in a 3' region to create or destroy a pseudo-ORF.

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8. A method for modulating the expression of a genetic sequence wherein said sequence comprises an ORF having an ATG or AUG corresponding to an authentic translation site of said ORF and a nucleotide sequence 5' of said authentic translation start site, said method comprising introducing or removing one or more ATG or AUG triplets in said 5' nucleotide sequence upstream of said authentic translation initiation site such that upon expression of said genetic sequence, there is a respective decrease or increase in the level of expression.

9. A method according to Claim 1 or 8 wherein the genetic sequence is DNA.

10. A method according to Claim 1 or 8 wherein the genetic sequence is RNA.

11. A method according to any one of Claims 8 to 10 further comprising introducing or removing one or more termination signals in the 5' nucleotide sequence, the coding sequence or downstream of the authentic translation initiation site and/or in a 3' region to create or destroy a pseudo-ORF.

12. A method for modulating the expression of a genetic sequence wherein said sequence comprises an ORF having an RTG corresponding to an authentic translation initiation site of said ORF where R is A or G and a nucleotide sequence 5' of said authentic translation initiation site, said method comprising introducing or removing one or more RTG triplets in said 5' nucleotide sequence upstream of said authentic translation initiation site such that upon expression of said genetic sequence, there is a respective decrease or increase in the level of expression.

13. A method according to Claim 12 wherein the expression is increased by the removal of one or more RTG triplets, wherein R is A or G in the 5' nucleotide sequence upstream of the authentic translation initiation site.

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14. A method according to Claim 12 wherein the expression is decreased by the introduction of one or more RTG triplets, wherein R is A or G in the 5' nucleotide sequence upstream of the authentic translation initiation site.

15. A method according to Claim 12 or 13 or 14 wherein the RTG triplets in the 5' nucleotide sequence upstream of the authentic translation initiation site is ATG.

16. A method according to any one of Claims 12 to 15 further comprising introducing or removing one or more termination signals in the 5' nucleotide sequence, the coding sequence or downstream of the authentic translation initiation site and/or in a 3' region to create or destroy a pseudo-ORF.

17. A method for modulating the expression of a genetic sequence wherein said sequence comprises an ORF having an RUG corresponding to a translation initiation site of said ORF where R is A or G and a nucleotide sequence 5' of said translation start site, said method comprising introducing or removing one or more RUG triplets in said 5' nucleotide sequence upstream of said authentic translation initiation site such that upon expression of said genetic sequence, there is a respective decrease or increase in the level of expression.

18. A method according to Claim 16 wherein the expression is increased by the removal of one or more RUG triplets, wherein R is A or G in the 5' nucleotide sequence upstream of the authentic translation initiation site.

19. A method according to Claim 16 wherein the expression is decreased by the introduction of one or more RUG triplets, wherein R is A or G in the 5' nucleotide sequence upstream of the authentic translation initiation site.

20. A method according to Claim 16 or 17 or 18 wherein the RUG triplets in the 5' nucleotide sequence upstream of the authentic translation initiation site is AUG.

21. A method according to any one of Claims 17 to 20 further comprising introducing or removing one or more termination signals in the 5' nucleotide sequence, the coding sequence or downstream of the authentic translation initiation site and/or in a 3' region to create or destroy a pseudo-ORF.
22. A method for facilitating increased or elevated expression of a genetic sequence wherein said sequence comprises an ORF having an RTG or RUG wherein R is A or G corresponding to an authentic translation initiation site of said ORF and a nucleotide sequence 5' of said authentic translation initiation site, said method comprising removing one or more RTG or RUG triplets in said 5' nucleotide sequence upstream of said authentic translation initiation site such that upon expression of said genetic sequence, there is an increase in the level of expression relative to expression of the genetic sequence in the absence of removal of any RTG or RUG triplet.
23. A method according to Claim 22 wherein the triplet removed from the nucleotide sequence 5' of the authentic translation initiation site is ATG.
24. A method according to Claim 22 wherein the triplet removed from the nucleotide sequence 5' of the authentic translation initiation site is AUG.
25. A method according to any one of Claims 22 to 24 further comprising introducing or removing one or more termination signals in the 5' nucleotide sequence, the coding sequence or downstream of the authentic translation initiation site and/or in a 3' region to create or destroy a pseudo-ORF.
26. A method for facilitating increased or elevated expression of a genetic sequence wherein said sequence comprises an ORF having an RTG wherein R is A or G corresponding to An authentic translation initiation site of said ORF and a nucleotide sequence 5' of said authentic translation initiation site, said method comprising removing

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one or more RTG triplets in said 5' nucleotide sequence upstream of said authentic translation initiation site such that upon expression of said genetic sequence, there is an increase in the level of expression relative to expression of the genetic sequence in the absence of removal of any RTG triplet.

27. A method according to Claim 26 wherein the triplet removed from the nucleotide sequence 5' of the authentic translation initiation site is ATG.

28. A method according to any one of Claims 26 or 27 further comprising introducing or removing one or more termination signals in the 5' nucleotide sequence, the coding sequence or downstream of the authentic translation initiation site and/or in a 3' region to create or destroy a pseudo-ORF.

29. A method for facilitating increased or elevated expression of a genetic sequence wherein said sequence comprises an ORF having an RUG wherein R is A or G corresponding to an authentic translation initiation site of said ORF and a nucleotide sequence 5' of said authentic translation initiation site, said method comprising removing one or more RUG triplets in said 5' nucleotide sequence upstream of said authentic translation initiation site such that upon expression of said genetic sequence, there is an increase in the level of expression relative to expression of the genetic sequence in the absence of removal of any RUG triplet.

30. A method according to Claim 29 wherein the triplet removed from the nucleotide sequence 5' of the authentic translation initiation site is AUG.

31. A method according to any one of Claims 29 or 30 further comprising introducing or removing one or more termination signals in the 5' nucleotide sequence, the coding sequence or downstream of the authentic translation initiation site and/or in a 3' region to create or destroy a pseudo-ORF.

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32. A method for facilitating decreased or reduced expression of a genetic sequence wherein said sequence comprises an ORF having an RTG or RUG where R is A or G corresponding to an authentic translation initiation site of said ORF and a nucleotide sequence 5' of said authentic translation initiation site, said method comprising introducing or creating one or more RTG or RUG triplets in said 5' nucleotide sequence upstream of said authentic translation initiation site such that upon expression of said genetic sequence there is a decrease in the level of expression relative to expression of the genetic sequence in the absence of introducing or removing any RTG or RUG triplets.

33. A method according to Claim 32 wherein the triplet removed from the nucleotide sequence 5' of the authentic translation initiation site is ATG.

34. A method according to Claim 32 wherein the triplet removed from the nucleotide sequence 5' of the authentic translation initiation site is AUG.

35. A method according to any one of Claims 32 to 34 further comprising introducing or removing one or more termination signals in the 5' nucleotide sequence, the coding sequence or downstream of the authentic translation initiation site and/or in a 3' region to create or destroy a pseudo-ORF.

36. A method for facilitating decreased or reduced expression of a genetic sequence wherein said sequence comprises an ORF having an RTG where R is A or G corresponding to an authentic translation initiation site of said ORF and a nucleotide sequence 5' of said authentic translation initiation site, said method comprising introducing or creating one or more RTG triplets in said 5' nucleotide sequence upstream of said authentic translation initiation site such that upon expression of said genetic sequence there is a decrease in the level of expression relative to expression of the genetic sequence in the absence of introducing or removing any RTG triplets.

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37. A method according to Claim 36 wherein the triplet introduced or created in the nucleotide sequence 5' of the authentic translation initiation site is ATG.

38. A method according to any one of Claims 36 or 37 further comprising introducing or removing one or more termination signals in the 5' nucleotide sequence, the coding sequence or downstream of the authentic translation initiation site and/or in a 3' region to create or destroy a pseudo-ORF.

39. A method for facilitating decreased or reduced expression of a genetic sequence wherein said sequence comprises an ORF having an RUG where R is A or G corresponding to an authentic translation initiation site and a nucleotide sequence 5' of said authentic translation initiation site of said ORF, said method comprising introducing or creating one or more RUG triplets in said 5' nucleotide sequence upstream of said authentic translation initiation site such that upon expression of said genetic sequence there is a decrease in the level of expression relative to expression of the genetic sequence in the absence of introducing or removing any RUG triplets.

40. A method according to Claim 39 wherein the triplet introduced or created in the nucleotide sequence 5' of the authentic translation initiation site is AUG.

41. A method according to any one of Claims 39 or 40 further comprising introducing or removing one or more termination signals in the 5' nucleotide sequence, the coding sequence or downstream of the authentic translation initiation site and/or in a 3' region to create or destroy a pseudo-ORF.

42. A method for modulating the expression of a genetic sequence wherein said sequence comprises an ORF having an RTG or RUG corresponding to an authentic translation initiation site and a nucleotide sequence 5' of said authentic translation start site comprising the sequence:-

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$$\{n_1 n_2 \dots n_a\}_m [x_1 x_2 x_3]_n \{n_1^I n_2^I \dots n_b^I\}_o [y_1^I y_2^I y_3^I] \{x_1^I x_2^I x_3^I\}_p [n_1^{II} n_2^{II} \dots n_c^{II}]_q \{y_1^{II} y_2^{II} y_3^{II}\} \\ [x_1^{II} x_2^{II} x_3^{II}]_r \{n_1^{III} n_2^{III} \dots n_d^{III}\}_s [y_1^{III} y_2^{III} y_3^{III}] \text{RT/UG} [z_1 z_2 \dots z_n]_t$$

wherein:

RT/UG is the authentic translation initiation site and R is A or G;

n , n^I , n^{II} and n^{III} are nucleotides selected from A, T or U, C or G or I;

$\{n_1 n_2 \dots n_a\}_m$, $\{n_1^I n_2^I \dots n_b^I\}_o$, $\{n_1^{II} n_2^{II} \dots n_c^{II}\}_q$ and $\{n_1^{III} n_2^{III} \dots n_d^{III}\}_s$ represent nucleotide sequences of a, b, c or d nucleotides in length and where each of n , n^I , n^{II} and n^{III} may be the same or different and its position is indicated by the subscript numeral 1, 2, ...;

$[z_1 z_2 \dots z_n]_t$ represents a translation termination signal within an authentic ORF but not in the same reading frame as said authentic ORF;

each of m, n, o, p, q, r or s may be the same or different and each is 0 or 1 or if there is a repeat or multiple repeats, from about 2 or about 10;

t is 0, 1 or >1;

each of $[x_1 x_2 x_3]_n$, $[x_1^I x_2^I x_3^I]_p$ and $[x_1^{II} x_2^{II} x_3^{II}]_r$ is selected from the triplet RTG, RUG, RYG, RTY^I, RY^{II}G, RUY^{III}, ATG, GTG, AUG and GUG where R is A or G, and each of Y, Y^I, Y^{II} and Y^{III} may be the same or different and each is a nucleotide with the proviso that Y is not T, Y^I is not G, Y^{II} is not U and Y^{III} is not G;

each of $[y_1^I y_2^I y_3^I]$, $[y_1^{II} y_2^{II} y_3^{II}]$ and $[y_1^{III} y_2^{III} y_3^{III}]$ represents a translation termination signal; and

said method comprising altering the nucleotide triplets $[x_1 x_2 x_3]_n$, $[x_1^I x_2^I x_3^I]_p$ and/or $[x_1^{II} x_2^{II} x_3^{II}]_r$ to introduce or remove an RTG or RUG to thereby respectively decrease or increase the level of expression of said genetic sequence.

43. A method according to Claim 42 wherein the genetic sequence is DNA

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44. A method according to Claim 42 wherein the genetic sequence is RNA.
45. A method according to Claim 42 or 43 or 44 wherein the nucleotide sequence 5' of the authentic translation initiation site is:-

$$n_x n_{x+i} \dots n_{x+z}$$

wherein:

n_x is the first nucleotide in a leader sequence;

x is 1 or >1 (e.g. 100, 1000, 10,000 or greater);

i is 1;

z is an integer from 1 to 10;

n_{x+z} is the last nucleotide of the 5' leader sequence prior to the translation initiation site;

wherein each n may be the same or different and each is A, C, G, U or T

and wherein a numerical value (N_V) is assigned to a genetic element such that if:-

n_{x+i} = n, as defined above;

n_{x+i+1} = A;

n_{x+i+2} = T or U; and

n_{x+i+3} = G

then the N_V is 1;

when

n_{x+j} = n, as defined above;

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$$\begin{aligned} n_{x+i+1} &= G; \\ n_{x+i+2} &= T \text{ or } U; \text{ and} \\ n_{x+i+3} &= G \end{aligned}$$

then the N_V is 0.3;

and when:-

$$\begin{aligned} n_{x+i} &= n \text{ as defined above;} \\ n_{x+i+1} &= C \text{ or } G; \\ n_{x+i+2} &= T \text{ or } C \text{ or } G; \text{ and} \\ n_{x+i+3} &= A, T \text{ or } C \end{aligned}$$

then the N_V is 0;

such that the level of expression (E_L) of a nucleotide sequence operably linked at its 5' end to $n_x n_{x+1} \dots n_{x+z}$ is inversely functionally associated (*) to the sum of N_V determined from the nucleotide sequence $n_x n_{x+1} \dots n_{x+z}$ such that

$$E_L * \frac{1}{\sum N_V}.$$

46. A method according to Claim 42 or 45 wherein the nucleotide sequence 5' of the authentic translation initiation site is derived from the *GLII* gene leader sequence.

47. A method according to Claim 46 wherein the *GLII* gene leader sequence is derived from a murine animal and comprises the nucleotide sequence set forth in SEQ ID NO:1 or a nucleotide sequence having at least 60% similarity thereto or a nucleotide sequence capable of hybridizing to SEQ ID NO:1 or its complementary form under low stringency conditions.

48. A method according to Claim 46 wherein the *GLII* gene leader sequence is derived from a murine animal and comprises the nucleotide sequence set forth in SEQ ID NO:1 or a nucleotide sequence having at least 60% similarity thereto or a nucleotide sequence capable of hybridizing to SEQ ID NO:2 or its complementary form under low stringency conditions.

49. A method according to Claim 46 wherein the *GLII* gene leader sequence is derived from a murine animal and comprises the nucleotide sequence set forth in SEQ ID NO:1 or a nucleotide sequence having at least 60% similarity thereto or a nucleotide sequence capable of hybridizing to SEQ ID NO:3 or its complementary form under low stringency conditions.

50. A method according to Claim 46 wherein the *GLII* gene leader sequence is derived from a human and comprises the nucleotide sequence set forth in SEQ ID NO:1 or a nucleotide sequence having at least 60% similarity thereto or a nucleotide sequence capable of hybridizing to SEQ ID NO:4 or its complementary form under low stringency conditions.

51. A method according to Claim 46 wherein the *GLII* gene leader sequence is derived from a human comprises the nucleotide sequence set forth in SEQ ID NO:1 or a nucleotide sequence having at least 60% similarity thereto or a nucleotide sequence capable of hybridizing to SEQ ID NO:5 or its complementary form under low stringency conditions.

52. An isolated nucleic acid for use in modulating the expression of a genetic sequence wherein said genetic sequence comprises a coding region comprising a translation initiation site and optionally a 5' leader sequence such that said nucleotide sequence comprising a predetermined number of RTG or RUG triplets such that upon operable linkage to the 5' end of the genetic sequence, the level of expression of said

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genetic sequence is determined by the number of RTG/RUG triplets.

53. A method according to Claim 52 wherein the triplet in the 5' leader sequence is ATG.

54. A method according to Claim 52 wherein the triplet in the 5' leader sequence is AUG.

55. A nucleic acid molecule according to Claim 53 or 54 wherein the nucleotide sequence 5' of the authentic translation initiation site is derived from the *GLII* gene leader sequence.

56. A nucleic acid molecule according to Claim 55 wherein the *GLII* gene leader sequence is derived from a murine animal and comprises the nucleotide sequence set forth in SEQ ID NO:1 or a nucleotide sequence having at least 60% similarity thereto or a nucleotide sequence capable of hybridizing to SEQ ID NO:1 or its complementary form under low stringency conditions.

57. A nucleic acid molecule according to Claim 55 wherein the *GLII* gene leader sequence is derived from a murine animal and comprises the nucleotide sequence set forth in SEQ ID NO:1 or a nucleotide sequence having at least 60% similarity thereto or a nucleotide sequence capable of hybridizing to SEQ ID NO:2 or its complementary form under low stringency conditions.

58. A nucleic acid molecule according to Claim 55 wherein the *GLII* gene leader sequence is derived from a murine animal and comprises the nucleotide sequence set forth in SEQ ID NO:1 or a nucleotide sequence having at least 60% similarity thereto or a nucleotide sequence capable of hybridizing to SEQ ID NO:3 or its complementary form under low stringency conditions.

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59. A nucleic acid molecule according to Claim 55 wherein the *GLII* gene leader sequence is derived from a human and comprises the nucleotide sequence set forth in SEQ ID NO:1 or a nucleotide sequence having at least 60% similarity thereto or a nucleotide sequence capable of hybridizing to SEQ ID NO:4 or its complementary form under low stringency conditions.

60. A nucleic acid molecule according to Claim 55 wherein the *GLII* gene leader sequence is derived from a human comprises the nucleotide sequence set forth in SEQ ID NO:1 or a nucleotide sequence having at least 60% similarity thereto or a nucleotide sequence capable of hybridizing to SEQ ID NO:5 or its complementary form under low stringency conditions.

61. A genetic construct comprising a promoter linked to a genetic element and one or more restriction endonuclease sites to facilitate insertion of a nucleotide sequence to be expressed by said promoter wherein said genetic element comprises a predetermined number of pseudo-translation initiation RTG/RUG triplets wherein R is A or G such that the level of expression of said nucleotide sequence by said promoter is inversely functionally associated with the number of RTG/RUG triplets in said genetic element.

62. A genetic construct according to Claim 61 wherein the genetic element comprises the nucleotide sequence:-

$$n_x n_{x+i} \dots n_{x+z}$$

wherein:

- n_x is the first nucleotide in a leader sequence;
- x is 1 or >1 (e.g. 100, 1000, 10,000 or greater);
- i is 1;
- z is an integer from 1 to 10;

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n_{x+z} is the last nucleotide of the 5' leader sequence prior to the translation initiation site;

wherein each n may be the same or different and each is A, C, G, U or T or I

and wherein a numerical value (N_V) is assigned to a genetic element such that if:-

$$\begin{aligned} n_{x+i} &= n, \text{ as defined above;} \\ n_{x+i+1} &= A; \\ n_{x+i+2} &= T \text{ or } U; \text{ and} \\ n_{x+i+3} &= G \end{aligned}$$

then the N_V is 1;

when

$$\begin{aligned} n_{x+i} &= n, \text{ as defined above;} \\ n_{x+i+1} &= G; \\ n_{x+i+2} &= T \text{ or } U; \text{ and} \\ n_{x+i+3} &= G \end{aligned}$$

then the N_V is 0.3;

and when:-

$$\begin{aligned} n_{x+i} &= n \text{ as defined above;} \\ n_{x+i+1} &= C \text{ or } G; \\ n_{x+i+2} &= T \text{ or } C \text{ or } G; \text{ and} \\ n_{x+i+3} &= A, T \text{ or } C \end{aligned}$$

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then the N_V is 0;

such that the level of expression (E_L) of a nucleotide sequence operably linked at its 5' end to $n_x n_{x+1} \dots n_{x+z}$ is inversely functionally associated (*) to the sum of N_V determined from the nucleotide sequence $n_x n_{x+1} \dots n_{x+z}$ such that

$$E_L * \frac{1}{\sum N_V}.$$

63. A genetic construct molecule according to Claim 62 wherein the genetic element comprises 5' leader sequence from the *GLII* gene.

64. A genetic construct according to Claim 63 wherein the *GLII* gene leader sequence is derived from a murine animal and comprises the nucleotide sequence set forth in SEQ ID NO:1 or a nucleotide sequence having at least 60% similarity thereto or a nucleotide sequence capable of hybridizing to SEQ ID NO:1 or its complementary form under low stringency conditions.

65. A genetic construct according to Claim 63 wherein the *GLII* gene leader sequence is derived from a murine animal and comprises the nucleotide sequence set forth in SEQ ID NO:1 or a nucleotide sequence having at least 60% similarity thereto or a nucleotide sequence capable of hybridizing to SEQ ID NO:2 or its complementary form under low stringency conditions.

66. A genetic construct according to Claim 63 wherein the *GLII* gene leader sequence is derived from a murine animal and comprises the nucleotide sequence set forth in SEQ ID NO:1 or a nucleotide sequence having at least 60% similarity thereto or a nucleotide sequence capable of hybridizing to SEQ ID NO:3 or its complementary form under low stringency conditions.

67. A genetic construct according to Claim 63 wherein the *GLII* gene leader sequence is derived from a human and comprises the nucleotide sequence set forth in SEQ ID NO:1 or a nucleotide sequence having at least 60% similarity thereto or a nucleotide sequence capable of hybridizing to SEQ ID NO:4 or its complementary form under low stringency conditions.

68. A genetic construct according to Claim 63 wherein the *GLII* gene leader sequence is derived from a human comprises the nucleotide sequence set forth in SEQ ID NO:1 or a nucleotide sequence having at least 60% similarity thereto or a nucleotide sequence capable of hybridizing to SEQ ID NO:5 or its complementary form under low stringency conditions.

69. A method for modulating expression of a genetic sequence which genetic sequence comprises an ORF with an authentic translation initiation site and further comprising a sequence upstream of said authentication translation initiation site where said method comprises introducing, creating or removing one or more pseudo-translation initiation triplets having the structure RWG wherein R is A or G and W is T or U in combination with introducing, creating or removing a Kozac or Kozac-like sequence proximal to said RWG such that the number of RWG triplets and Kozac or Kozac-like sequences is inversely functionally associated with expression of said genetic sequence.

70. A method according to Claim 69 wherein the pseudo-translation initiation triplet is ATG.

71. A method according to Claim 69 wherein the pseudo-translation initiation triplet is GTG.

72. A method according to Claim 69 wherein the pseudo-translation initiation triplet is AUG.

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73. A method according to Claim 69 wherein the pseudo-translation initiation triplet is GUG.

74. A method according to Claim 69 wherein the introduction, creation or removal of a pseudo-translation initiation triplet creates the sequence:-

RnCCRWGn [SEQ ID NO:11]

wherein:-

R is A or G;

n is any nucleotide; and

W is T or U.

75. A method for modulating the expression of a genetic sequence in a plant cell wherein said sequence comprises an ORF having an RTG or RUG wherein R is A or G corresponding to an authentic translation site of said ORF and a nucleotide sequence 5' of said authentic translation start site, said method comprising introducing or removing one or more RTG or RUG triplets in said 5' nucleotide sequence upstream of said authentic translation initiation site such that upon expression of said genetic sequence, there is a respective decrease or increase in the level of expression.

76. A method according to Claim 75 wherein the expression is increased by the removal of one or more RTG or RUG triplets, wherein R is A or G in the 5' nucleotide sequence upstream of the authentic translation initiation site.

77. A method according to Claim 75 wherein the expression is decreased by the introduction of one or more RTG or RUG triplets, wherein R is A or G in the 5' nucleotide sequence upstream of the authentic translation initiation site.

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78. A method according to Claim 75 or 76 or 77 wherein the RTG or RUG triplets in the 5' nucleotide sequence upstream of the authentic translation initiation site is ATG or AUG.

79. A method according to Claim 78 wherein the triplet is ATG.

80. A method according to Claim 78 wherein the triplet is AUG.

81. A method according to any one of Claims 75 to 80 further comprising introducing or removing one or more termination signals in the 5' nucleotide sequence, the coding sequence or downstream of the authentic translation initiation site and/or in a 3' region to create or destroy a pseudo-ORF.

82. A method according to Claim 75 or 81 wherein the plant cell is from a cereal crop, a vegetable plant, a fruiting plant, a flowering plant or cotton or tobacco. ✓

83. A method according to Claim 82 wherein the plant cell is from cotton.

84. A method according to Claim 82 wherein the plant cell is from a cereal crop.

85. A method according to Claim 82 or 83 or 84 wherein the target sequence whose expression is modulated confers resistance to a herbicide.

86. A method according to Claim 82 or 83 or 84 wherein the target sequence whose expression is modulated confers resistance to a pesticide.

87. A method for modulating the expression of a genetic sequence in an animal cell wherein said sequence comprises an ORF having an RTG or RUG wherein R is A or G corresponding to an authentic translation site of said ORF and a nucleotide sequence 5' of

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said authentic translation start site, said method comprising introducing or removing one or more RTG or RUG triplets in said 5' nucleotide sequence upstream of said authentic translation initiation site such that upon expression of said genetic sequence, there is a respective decrease or increase in the level of expression.

88. A method according to Claim 87 wherein the expression is increased by the removal of one or more RTG or RUG triplets, wherein R is A or G in the 5' nucleotide sequence upstream of the authentic translation initiation site.

89. A method according to Claim 87 wherein the expression is decreased by the introduction of one or more RTG or RUG triplets, wherein R is A or G in the 5' nucleotide sequence upstream of the authentic translation initiation site.

90. A method according to Claim 87 or 88 or 89 wherein the RTG or RUG triplets in the 5' nucleotide sequence upstream of the authentic translation initiation site is ATG or AUG.

91. A method according to Claim 90 wherein the triplet is ATG.

92. A method according to Claim 90 wherein the triplet is AUG.

93. A method according to any one of Claims 87 to 92 further comprising introducing or removing one or more termination signals in the 5' nucleotide sequence, the coding sequence or downstream of the authentic translation initiation site and/or in a 3' region to create or destroy a pseudo-ORF.

94. A method according to Claim 87 or 93 wherein the animal cell is a mammalian cell.

95. A method according to Claim 87 or 93 wherein the animal cell is a human cell.